CLAIMS:

1. A method of preparing a heteromultimer comprising a first polypeptide and a second polypeptide which meet at an interface, wherein the interface of the first polypeptide comprises a protuberance which is positionable in a cavity in the interface of the second polypeptide, the method comprising the steps of:

(a) culturing a host cell comprising nucleic acid encoding the first polypeptide and second polypeptide, wherein the nucleic acid encoding the first polypeptide has been altered from the original nucleic acid to encode the protuberance or the nucleic acid encoding the second polypeptide has been altered from the original nucleic acid to encode the cavity, or both, and wherein the culturing is such that the nucleic acid is expressed; and

(b) recovering the heteromultimer from the host cell culture.

2. The method of claim 1 wherein the nucleic acid encoding the first polypeptide has been altered from the original nucleic acid to encode the protuberance and the nucleic acid encoding the second polypeptide has been altered from the original nucleic acid to encode the cavity.

3. The method of claim 1 wherein step (a) is preceded by a step wherein nucleic acid encoding an original residue from the interface of the first polypeptide is replaced with nucleic acid encoding an import residue having a larger side chain volume than the original residue.

4. The method of claim 3 wherein the import residue is arginine (R).

5. The method of claim 3 wherein the import residue is phenylalanine (F).

6. The method of claim 3 wherein the import residue is tyrosine (Y).

7. The method of claim 3 wherein the import residue is tryptophan (W).

8. The method of claim 1 wherein step (a) is preceded by a step wherein nucleic acid encoding an original residue in the interface of the second polypeptide is replaced with nucleic acid encoding an import residue having a smaller side chain volume than the original residue.

9. The method of claim 8 wherein the import residue is not cysteine (C).

10. The method of claim 8 wherein the import residue is alanine (A).

11. The method of claim 8 wherein the import residue is serine (S).

12. The method of claim 8 wherein the import residue is threonine (T).

13. The method of claim 8 wherein the import residue is valine (V).

14. The method of claim 1 wherein the first and second polypeptide each comprise an antibody constant domain.

15. The method of claim 14 wherein the antibody constant domain is a $C_H3$ domain.

16. The method of claim 15 wherein the antibody constant domain is from an IgG.

17. The method of claim 16 wherein the IgG is human $IgG_1$.

18. The method of claim 1 wherein the heteromultimer is a bispecific antibody.

(b) altering a second nucleic acid encoding a second polypeptide so that an amino acid residue in the interface of the second polypeptide is replaced with an amino acid residue having a smaller side chain volume, thereby generating a cavity in the second polypeptide, wherein the protuberance is positionable in the cavity;

(c) introducing into a host cell the first and second nucleic acids and culturing the cell so that expression of the first and second nucleic acid occurs;

(d) recovering the heteromultimer formed from the cell culture.

36. The method of claim 35 wherein the first and second polypeptide each comprise an antibody constant domain.

37. The method of claim 35 wherein the antibody constant domain is a $C_H3$ domain.

38. The method of claim 37 wherein the antibody constant domain is from a human IgG.